

### REMARKS

Claims 77, 78, 80, 84, 87-88, 105-106, 114-115, 128 and 133-134 are currently pending in this application.

The specification has been objected to based on certain discrepancies concerning the numbering of the amino acid and nucleic acid positions in the wild-type and mutant LFA-1 sequence. The numbering system used in Table 9 has also been questioned.

With regard to the Declaration of Dr. Shimaoka, the Examiner states that the Declaration fails to provide evidence that the mature LAF-1 protein is 25 amino acids less than the precursor protein. Such evidence could be based on a published sequence, for instance.

Accordingly, enclosed with this amendment is a copy of the following publication: Larson et al., *The Journal of Cell Biology*, Vol. 108, pages 703-712 (1989). This publication discloses the complete LFA-1 mature native sequence, including the signal sequence which is shown underlined with a thick line for convenience. The numbering of the amino acid positions in the mature protein are shown on the left hand side of the sequence, which also shows the signal sequence. A copy of the publication is enclosed.

In response, applicants state that precursor  $\alpha$ L protein is shown in SEQ ID. NO:1 and SEQ ID NO:2. These sequences include the additional 25 amino acids present in the precursor protein. After cleavage of the signal sequence, the mature protein does not contain the signal sequence as shown (underlined) in the Larson et al. publication.

The numbering system used in the present specification to denote the mutations listed in Table 9 is based on the mature protein. Thus, the numbering system used in Table 9 for the listed mutations is 25 amino acids less than the corresponding positions found in the precursor protein depicted in SEQ ID NO:2. The claims have also been amended in order to specify that the numbering system used for the mutations is based on the mature form of the  $\alpha$ L protein.

Claims 77, 78, 80, 84, 87-88, 105-106, 114-115, 128 and 133-134 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which is not described in the specification

so as to enable one skilled in the art to practice the invention, or to convey the fact that applicants had possession of the invention.

The Office Action states that the claims refer to the  $\alpha$ L precursor protein, while the amino acid substitutions are directed to the mature form of the protein.

The claims have now been amended to recite that the numbering system for the substitutions is based on the mature protein. Consequently, it is submitted that this rejection has been overcome.

Claims 77, 78, 80, 84, 87-88, 105-106, 114-115, 128 and 133-134 also stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the invention.

Applicants respectfully submit that this rejection has been obviated as a result of the claim amendments discussed above.

In view of the aforementioned facts and reasons, the pending claims of this application are now believed to overcome any remaining rejections, and to satisfy all requirements for patentability. This Amendment is deemed appropriate at this time since it is responsive to the Examiner's requests, and does not require any new search or consideration on the part of the Examiner. Accordingly, withdrawal and reconsideration of the rejections, and allowance of the claims in this application, are solicited. The Examiner is invited to contact the undersigned if this would serve to advance the prosecution of this application.

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